Building and assessment of Gastric Cancer Ontology

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Summary

Background: The gastric cancer is one of the main reasons of death. In addition, the incidence of various types of cancer, especially gastric cancer, is increasing today. The high levels of cancer data from different sources may be considered as an obstacle to the organization and management of knowledge in a particular region. In this regard, the ontology approach has attracted the attention of the researchers due to its ability to solve a variety of heterogeneous problems. This study aimed to design and implement gastric cancer ontology (StOnt); this may be considered as one of the main measures to control burden of this disease.

Methods: This was a developmental descriptive study; it describes those research components that include ontology concepts and relationships. The design and implementation process was carried out in seven steps combining methods employed in Damontier and Villa Viva Rosales, and guideline on developing good ontologies ontology in the biomedical domain. Data gathering was carried out over four months of 2018. The Protégé editor version 5.0.0 was also used as a tool to build the ontology.

Results: Resulting ontology includes all the specific concepts of gastric cancer (1146 axioms) and 17 object properties (relations). Validation of StOnt using named entity recognition-based methods and ProMiner software as a tool indicated that recall= 0/85, precision=0/90 and F score≥ 87% as well as the positive opinion of experts in structural and functional evaluation with suggesting 53 new axioms.

Conclusions: The increasing incidence of gastrointestinal cancers requires a greater determination to develop relevant ontologies, so the development of StOnt is the first effort to organize the relevant information that will continue.

Keywords:

Medical Records, Biological Ontologies, Stomach Neoplasms, Health Information Management, StOnt

1. Introduction

Among medical sub-domains, cancer is a complex group of diseases that affects a significant portion of the population around the world.(1) Cancer was responsible for 8.8 million deaths in 2015.(2)

According to World Health Organization (WHO), the most common causes of cancer death in 2015 are cancers of:

- Lung (1.69 million deaths)
- Liver (788 000 deaths)
- Colorectal (774 000 deaths)
- Stomach (754 000 deaths)
- Breast (571 000 deaths)(2)

Statistics show that due to the presence of various environmental contaminants, malnutrition, inactivity, and other pathogens, the incidence of various types of cancer, especially gastric cancer, is increasing today. Obviously, the amount of patient data has also increased, so for the effective use of these data, the cancer research community requires informatics methods that help researchers to search, access, and analyze related data, and thereby facilitate the realization of technology applications in personalized treatment methods.(3)

In the last decades the traditional knowledge organization tools such as classification programs, subject headings, thesauri, etc., mainly designed for printed medium, have been developed electronically due to extensive technological changes and are trying to fit into new environment. However, these tools have functional limitations in the organization of knowledge in electronic and web-based environment. Moreover, recently, various researchers in different fields of medical science (4-11) have significantly focused on development of ontology. In particular, ontologies, which include a common vocabulary and logical structure (information) are necessary because of providing the knowledge framework for scientific discourse, annotation, semantic integration, knowledge-based searching, mining, inferencing and unambiguous interpretation of data, natural language processing, knowledge retrieval, databases, knowledge management, online database integration, digital libraries, geographic information systems, image information retrieval, or multiprocessing systems.(3)

Therefore, given the above capabilities, the medical science specifically requires this kind of technology in organization of knowledge, as a basis for using new analytical tools in cancer research and in some cases, as a means of diagnosis and treatment.(12)

Although many terminologies and ontological resources have been developed in the biomedical field (6, 11, 13-16),

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it is still necessary to cover emerging sub-domains such as gastric (stomach) cancer of which knowledge of the domain is regularly enriched. Therefore, modeling relevant knowledge about the domain is an important issue for a better understanding of the disease and a better support for patients.

Given that, we require ontologies to demonstrate specific knowledge about the scope of gastric (stomach) cancer, so that they can be used to merge the meaning of different parts of the data, knowledge-based search and for drawing conclusions based on the logical classification of terms and relations between the terms provided by the ontology.

This study was conducted to develop the ontology of gastric cancer based on concepts and relationships in related resources.

In the face of the challenge of ontological construction and the required efforts to do so, the reuse of existing termino-ontological resources is still a very important issue, especially in the field of biomedicine, where large resources are available. Therefore, approaches can benefit from these resources to facilitate and accelerate the ontology development process. These techniques often attempt to capture the implicit meanings of these resources. In literature, many studies have focused on the reuse of existing resources for ontology engineering.

Dennis et al. in (10) have designed and developed a Nano-Particle Ontology (NPO) to facilitate the semantic integration, knowledge-based search, accurate interpretation, data extracting and inference. The NPO was designed based on the framework of the Basic Formal Ontology (BFO) version 1.1, and implemented in the Ontology Web Language (OWL) using well-defined ontology design principles. They started the construction of Nano-Particle Ontology by creating an initial list of terms pertaining to a general description of Nano-Particle in the literature. Then for editing OWL files, they used Protégé as an ontology editing software. Bright et al.4 developed an ontology for guiding appropriate antibiotic prescribing in six steps; define the ontology domain and scope: review existing ontologies; identify classes and properties; create a conceptual map; identify and implement an upper ontology; and implement the ontology in a formal representation. After representing the ontology in the Web Ontology Language (OWL) using the Protégé-OWL editor, they used a set of ontology design principles and domain expert review to measure ontology correctness in terms of structure and content.

Drame and their colleagues 6 combine two methods: ontology learning from texts and the reuse of existing terminological sources in four steps. These steps include (I) term extraction from domain specific corpora using textual analysis tools, (II) clustering of terms into concepts organized according to the Unified Medical Language System (UMLS) meta-thesaurus, (III) ontology enrichment through the alignment of French and English terms using parallel corpora and the integration of new concepts, (IV) refinement and validation of results by domain experts. These validated results are formalized into a domain ontology dedicated to Alzheimer's disease and related syndromes by the Protégé editor tool.

In (17) researchers have designed AgroPortal, an ontology repository for the agronomy domain, reusing the National Center for Biomedical Ontologies (NCBO) BioPortal technology. The AgroPortal project reuses the semantic tools of the biomedical field and insights to serve agronomy, but also food, plant, and biodiversity sciences. They used the conceptual framework for knowledge in the ontology, which is based on well-established ontologies in plant sciences such as Gene Ontology, Sequence Ontology, Plant Ontology, Crop Ontology and Plant Environment Ontology. Finally, they provide a portal that features ontology hosting, search, versioning, visualization, comment, and recommendation; enabling semantic annotation; storing and exploiting ontology coordination; and enabling collaboration with the semantic web.

In this way, developing StOnt help specialists in organizing medical records to have best practice in their domain, facilitating communication between cancer researchers, ensuring the semantic interaction between programs and databases, and creating a basis for using new analytical tools in cancer research.

2. Materials and Methods

This was developmental study; it addressed the method and stages of designing, developing and evaluating gastric cancer ontology (StOnt). The results of using each of these methods are presented in the section 4 (Design and implementation of StOnt) and section 6 (evaluation of StOnt).

2.1 The Development of Ontology

The development of StOnt was conducted with a combination of methods used in Dumontier &, Villanueva-Rosales (18) and Guideline for developing good ontology (19) in seven phases. To this end, the concepts and relationships of gastric cancer were extracted from:

a. related web sites and databases,
b. 500 medical records produced from 2013 to 2018 (C 16.0- C 16.9 based on International Classification of Disease (ICD-10)) existing in Yazd Shahid Sadoughi hospital (governmental) which were selected randomly,
c. scientific studies in PubMed and Up To Date (2012-2018) and
d. Medical Subject Headings (MeSH)

using the knowledge engineering approach. Then, the extracted concepts and relationships were entered into Protégé 5.0.0 (20) software.

2.2 Evaluation of Ontology

Named entity recognition-based methods and domain expert survey were used to validate the lexicalized ontology and measure ontology integrity in terms of structure and content. Therefore, StOnt was evaluated in two stages.

2.3 Terminology Analysis

In order to assess the lexicalized ontology in terms of measuring the boundaries of the knowledge domain that it captures precision, recall, and F-score values were calculated. For this aim Prominer software was used as a tool. These values were computed based on the terms match between set of terms used in 100 gastric cancer studies published since 2012, as a reference gold standard (937 terms were extracted) with the StOnt dictionary. The conversion of the ontology OWL format into a dictionary file was accomplished using a Java program that extracts the name of the concept and the corresponding synonyms from the ontology OWL structure and assigns unique identifiers to each concept that can be stored in form of a dictionary. The following equations, named entity recognition-based method, were used for the computation of recall, precision, and F-score values. (21)

$$\Pr ecision = \frac{True\ \ positives}{True\ \ positives + False\ \ positives}$$

$$\operatorname{Re} call = \frac{True\ \ positives}{True\ \ positives + False\ negatives}$$

$$F\ score = \frac{2 \times precision \times recall}{precision + recall}$$

Fig. 1: Entity recognition-based equation

In this equation, the true positives are the number of entities that matched between dictionary and reference gold standard; the false positives are the number of entities that were annotated in dictionary but could not be consistent with the annotations in the reference gold standard. The false negatives are the number of entities that were not found in dictionary compared to the manual reference gold standard annotation.

2.4 Expert Validation

In the second stage, the validity of ontology was examined based on oncologist's knowledge and experiences in specialized fields and following components. So in this qualitative approach, four semi structured interviews was held to receive their comments and suggestions.
Two specialists (working at the Yazd Shahid Sadoughi hospital) have evaluated StOnt. They received the ontology in present. Then they were asked to evaluate the StOnt according to the following components:

- A list of concepts in National Cancer Institute thesaurus (NCIt), associated with related terms. Accordingly, there may be better judgment about relationships (oncologist, Gastroenterologist).
- Non-taxonomic relationships deriving from NCIt and relevant ontologies at NCBO Bioportal (oncologist, Gastroenterologist).
- A list of words not found in NCIt, but available in medical records and added to StOnt (oncologist, Gastroenterologist).

A summary of the study can be seen in Figure 2.

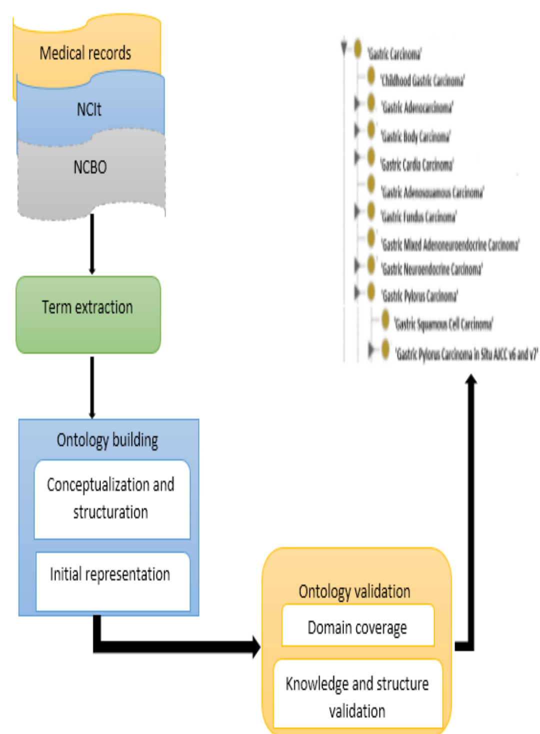

Fig. 2 Overview of the StOnt building method.

3. Results

The design and implementation of gastric cancer ontology was processed in the following steps:

a) Defining the scope and coverage of ontology: This includes all terms that refer to gastric cancer such as risk factors, involved tissues, therapeutic measures, and symptoms. The basis was semantic concepts and relationships.

b) Examining related ontologies: Prior to constructing the ontology, the biomedical literature and ontology repositories mentioned in "The Development of Ontology" section, were used as basic ontology to create preview of gastric cancer ontology and extract related terms along with synonyms and preferred and non-preferred terms hierarchically.

c) Identifying the conceptual pairs and their relationships: Here, using Knowledge Engineering approach, existing ontologies were examined; then, the conceptual pairs and their relationships were identified and the concepts and relationships were located in appropriate hierarchical and semantic position. This step was done to help organize and design ontology classes and features prior to implementing the ontology in a formal representation.

d) Determining classes and their hierarchy: Since National Cancer Institute's thesaurus, Cancer ontologies at NCBO Bioportal, and medical records were selected as basic ontologies, the cases in these resources were selected as classes. Moreover, the hierarchy between classes was determined according to hierarchy of thesaurus. The classification of concepts was carried out based on the conceptual system in thesaurus of National Cancer Institute. Each preferred term was considered as a concept or class, and "particular/ general" relationships were converted into "subclass/ top class" relationships. This means that if a concept is considered based on a term that is specific to another term, this concept will be a subclass of the concept which is considered by second term in ontology. Finally, these classes were included in class section at protégé. An example of classification used in StOnt is shown in figure 3.

e) Describing class slots (relationships): In particular, the information provided in classes is not sufficient. Therefore, the slots section is used for relationships required in ontology and the relationships between classes were created in this way; in this study, the "slots" section was used for this purpose. The slots section in protégé was completed with semantic relationships in the mentioned resources.

f) Defining facet of slots: The slots may have different facets. The slots facets specify the type of values, the permitted values, and their number. The facets are used in practice to define the boundaries and types of relationships between the samples. For example, the “treatment” feature may be used with specific examples. Therefore, a list of permitted classes that may have “treatment” relationships should be specified.

g) Creating instances: The last step is to create instances for each class. Defining class instances in the software requires selecting that class, creating a single instance, and filling the slots with specified and allowed values. In this research, the instances section was devoted to concepts. The conceptual pairs (stage "C") were included in the samples and the relationships were established among them based on the facets, which were identified at stage "six". The slots that are used to describe instances are mostly the name of sample, the equivalent concept in the National Cancer Institute's thesaurus, synonyms, and semantic relationships among samples.

h) After conceptual design of ontology and the study of common concepts and relationships between them and other concepts by thematic specialists, the implementation stage was carried out. At this stage, the conceptual design was implemented in the form of web ontology language (OWL) which is the recommended standard language of World Wide Web consortium for ontology; ultimately, the anthology of gastric cancer was created.

Protégé 5.0.0 (20) was used to formulate the ontology. The resulting ontology is consisted of 1146 entities, 17 object properties, and 6 data properties and is available in the OWL format. The semantic relationships “Is a”, “Has a”, “Part of”, “Associated with”, “Occurs in”, “Consists of”, “Indicates”, “Result of”, “Interconnects”, “Location of”, “Adjacent to”, “Affects”, “Diagnoses”, “Treats”, “Disrupts”, “Prevents” and “Causes” were used to define the type of relationship between pairs of concepts. The outstanding classes and definitions of the ontology are shown in Table I. The ontology will be available soon to the public.

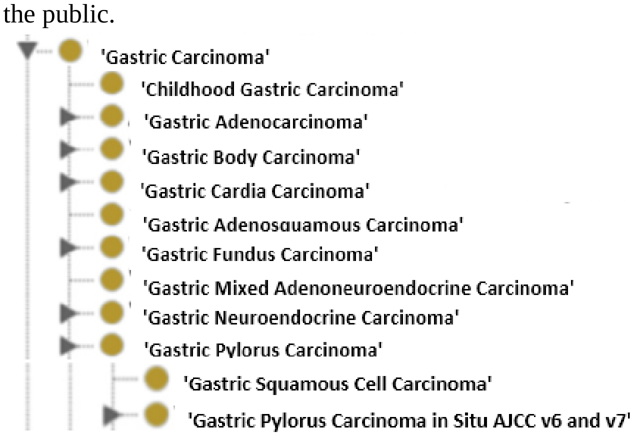

Fig. 3 Views extracted from StOnt along with the basic formal ontology (BFO)

Table 1: The outstanding classes and definition of StOnt

Class	Definition
Gastric cancer quiz	A diagnostic test establishes the presence of the disease
Gastroenterology	The medical specialty devoted to the study, diagnosis and treatment of disorders of the digestive system
Adenocarcinoma	Cancer that begins in glandular (secretory) cells.
Biopsy specimen	Tissue removed from the body and examined under a microscope to determine whether disease is present.
Chemotherapy	Treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.
Family history	A record of the relationships among family members along with their medical histories.
Gastric cancer	Cancer that forms in tissues lining the stomach. Also called stomach cancer.
Gastro scope	A thin, tube-like instrument used to examine the inside of the stomach.
Helicobacter pylori	A type of bacterium that causes inflammation and ulcers in the stomach or small intestine.
Pernicious anemia	A type of anemia (low red blood cell count) caused by the body's inability to absorb vitamin B12.

4. Evaluation of the StOnt

Ontology evaluation is specifically intended to measure the quality of ontologies, either to provide feedback to ontology developers and knowledge engineers or to provide insights into the adequacy of ontologies to their users. (22)

5. Domain Coverage

Confirmation of the domain coverage is essential to ensure that ontology is usable. There are many strategies to do this.(5) Functional evaluation measures how widely and precisely ontological concepts represent the semantic space for the indicated field of knowledge.(9) The knowledge domain coverage addressed by StOnt was estimated by calculating its fitness to related scientific studies. In this way, StOnt were evaluated effectively using named entity recognition-based method by ProMiner software and report an F score of 87%. The result of this assessment shows that ontology in its current form can capture a wide range of gastric cancer concepts in the field of knowledge throughout medical records.

$$fscore = \frac{2 * 0/90 * 0/85}{0/90 + 0/85}$$

Table 2: StOnt Functional Evaluation

	Precision	Recall	F score
Collection of 100 abstracts	0/90	0/85	0/87

6. Validation of Knowledge and Structure

The review of the panel of experts from the ontological view structure is considered as an assessment for disease ontologies.(23) It is worth pointing out that a eight-hour interview was scheduled with two specialists on weaknesses and strength of StOnt, based on their knowledge and experience in specialized fields and above-mentioned components. The interviews were scheduled and carried out in two-hour sessions in the summer 2018, as shown in Table 3, with the aim of preventing fatigue and thus reduction in the quality of the interviews. Ultimately, the candidate ontology (StOnt) was able to meet their expectations.

Table 3: The Schedule for interview

Sl. No	Specialty	Dates for interview	Addresses
1	Oncologist	20.05.2018 21.05.2018	Iran, Yazd, Shahid sadooghi hospital
2	Gastroenterologist	22.05.2018 23.05.2018	Iran, Yazd, Shahid sadooghi hospital

According to this evaluation, 53 new concepts were integrated to develop the initial ontology. Examples of new concepts integrated to improve StOnt are listed in Table 4.

Table 4: Some of new concepts and definitions, which have been added to StOnt after knowledge and structure validation

Added concepts	**Definitions**
Submucosal	A supporting layer of loose connective tissue directly under a mucous membrane — called also *tela submucosa*
Polyp	Projecting growth of tissue from a surface in the body, usually a mucous membrane.
Peptic ulcers	Sores that develop in the lining of the stomach, lower esophagus, or small intestine.
Fried food	Cooking of *food* in oil or another fat.
Pernicious anemia	A disease where large, immature, nucleated cells circulate in the blood, and do not function as blood cells; it is a disease caused by impaired uptake of vitamin B-12 due to the lack of intrinsic factor (IF) in the gastric mucosa.
Serosa	The visceral peritoneum covering the outer surface of the stomach

7. Discussion

Considering gastric cancer is the fourth deadly cancer (based on WHO statistics)(2) and absent of semantic technology solutions for better understanding the information obtained in the field, particularly from a conceptual perspective; present study attempts to design and implement the specific ontology entitled "StOnt" to improve the organization, search, versioning, establishing a relationship, and to retrieve of the knowledge. Studies show that StOnt is the first formal ontology in the field of gastric cancer (24), which has been important in terms of semantic technology due to the widespread prevalence of gastric cancer.

In order to make the ontology more comprehensive, relevant resources such as websites, published scientific studies, databases and medical records were studied, then related concepts were extracted. In this way Malhotra & their colleagues (9) have generated the collection of terms and concepts related to Alzheimer's Disease by scanning various knowledge sources including review articles, content of online books, standard knowledge bases, encyclopedias, glossaries, and informative online sources and websites.

During the course of construction of StOnt, special emphasis was applied to aspects of usability of the ontology. Although the used method is time-consuming, the researchers regard it as a valid and appropriate method for creating medical ontologies.

While, the review of various studies suggests a lack of a standard in the development of ontologies. (7, 25, 26) These conditions make researchers around the world examine different paths and methods for the development of the ontology. In this regard, development of StOnt was applied with a combination of previous methods used by Dumontier &, Villanueva-Rosales (18) and Guideline for developing good ontology (19) in seven phases. Bright et al.(4) used two guides (27, 28) to define a six-step development process for the antimicrobial-microorganism ontology. Tong etc. (29) at first have created a Traditional Chinese Medicine Language System thesaurus by searching and gathering terms from various sources (e.g., subject headings, classification schemes, dictionaries, papers, monographs, databases, etc.), which are distributed across different organizations, libraries, and data centers; then used the thesaurus for enriching Traditional Chinese Medicine Ontology.

Like diversity in ontology development methods, the researchers used a variety of methods and tools to assess their own ontology (9, 30-33) that assess various aspects of ontology. Here so, routine evaluations were carried out in terms of thematic scope coverage, structure and knowledge of the ontology; the results indicated F score=0/87 in the functional aspect of ontology, as well as the positive opinion of gastric cancer experts in the field of structural StOnt. In this regard, based on existing studies (9), F score higher than 70% indicates that ontology in valuable.

8. Conclusions

Cancer is a complex disease that affects a large population in the world. In addition, the coordinated and evidence-based care requires specific tools for communication and information technology such as distributed electronic folders, decision support systems (DSS), and workflow management tools. Meanwhile, due to the differences in the use of medical terminology and concepts among experts, it seems difficult to integrate these systems during clinical trials. In this regard, the biomedical informatics professionals are trying to use biomedical ontologies to overcome these problems and make better Information and Communication Technology (ICD) tools. The ontologies are considered as a solution to overcome the differences between different systems, given their ability to describe a transparent and machine-readable semantics.

This article was conducted on development and implementation of particular ontology for gastric cancer called "StOnt". In order to develop StOnt, the OWL template and BFO framework were used as a high-level ontology for systematically categorization of gastric cancer concepts. This ontology includes all the specific concepts of gastric cancer (1146 concepts) such as symptoms, risk factors, diagnostic and therapeutic methods, stages and location of disease, medications, therapeutic tools, and involved tissues. Moreover, we used other related ontologies to concept enrichment of the StOnt.

It should be noted that the StOnt was designed to meet the terminological needs of gastric cancer research, including enabling semantic coordination between various software and resources, exchange of data between oncologists, the provision of knowledge support for data annotation in order to facilitate semantic integration, knowledge-based search, unambiguous interpretation, mining, and input of data.

We suggest that, since data collected from related studies, ontologies should be developed using existing data from other health and research centers and related sites in order to identify the specific concepts covering and compare it with present ontology. In addition, it is suggested that using the various techniques and tools experimented for developing ontology, the creation and development of cancer-related ontologies with the highest mortality rates (according to WHO) such as liver and colorectal cancer should be put on the agenda of relevant researchers in the future. Given the opportunities that ontologies have created, it is possible to master the semantic differences between researchers and health field professionals, to integrate different clinical systems, and ultimately to reduce the burden of these diseases.

The application of the results of this article can be useful for managers and specialists in the organization of medical information.

Conflict of interest

The authors declare that they have no conflicts of interest in the research.

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